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with Special Reference to the Incidence and
Treatment of Amœbic Dysentery Carriers.



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A Study of 1,300 Convalescent Cases of Dysentery from Home Hospitals:

with special reference to the Incidence and
Treatment of Amœbic Dysentery Carriers.

BY

CLIFFORD DOBELL, M.A.
(*Imperial College of Science*).

H. S. GETTINGS, D.P.H.

MARGARET W. JEPPE
(*Bathurst Student, Newnham College, Cambridge*).

All working on behalf of the Medical Research Committee.

AND

J. B. STEPHENS, M.B., B.S., D.P.H.
(*Major, R.A.M.C. : Health Officer, Rangoon Municipality*).

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INTRODUCTION.

By

CLIFFORD DOBELL AND H. S. GETTINGS.

Towards the close of the year 1916 the War Office decided to open a temporary depôt for dysenteric patients in this country—a course necessitated by the increasingly large number of convalescent cases awaiting admission to the regular Dysentery Depôt at Barton-on-Sea. Accordingly, in November, 1916, the Manor (County of London) War Hospital at Epsom (Lieut.-Colonel W. Ireland Donaldson, R.A.M.C., commanding) was converted into a temporary dysentery depôt, and we were asked by the Medical Research Committee to assist the War Office in carrying out its plans by undertaking the bacteriological and protozoological examination of all cases admitted.

The depôt was soon in full running order, and our work of examining the stools of the inmates began in December, 1916, and continued until the early summer of 1917. During this time 1,300 cases passed through the depôt. At first our efforts were solely directed towards the detection of carriers. The stools of every case were examined by one of us (H. S. G.) for pathogenic bacilli, and by the other (C. D.) for protozoal infections. It soon became clear that the patients—who had all been previously discharged as “negative” from home hospitals—contained among them a fairly large proportion of carriers of the dysentery amoeba (*Entamoeba histolytica*); but no “positive” cases, and comparatively few interesting infections occurred to relieve the monotonous sequence of “negatives” obtained from the bacteriological examinations.

All the amoebic dysentery carriers found were detained and treated with emetine bismuth iodide; and they thus afforded an opportunity of testing, on a large scale, the efficacy of this drug in curing amoebic infections. After sorting out the “negative” cases from the whole series, therefore, the work at the depôt consisted chiefly in treating and re-examining the amoebic dysentery carriers. Fortunately, we obtained the services of Miss M. W. Jepps at the beginning of the year, and her collaboration from that time onwards has served to lighten considerably the very heavy work involved in examining the treated cases. This work came to an end in the summer of the past year, and the results obtained at the Epsom Dysentery Depôt during its brief existence (November, 1916, to July, 1917) are set forth in the following Report.

We have worked throughout in close collaboration with Major J. B. Stephens, R.A.M.C., who took entire medical charge of the patients at Epsom. Not only has he treated all the cases

whose treatments are dealt with in this Report, but he has also contributed all the clinical observations made upon them, and has been responsible throughout for the collection of information concerning the medical histories of the cases which we have studied together. At the outset, it was found impossible for us to make the necessary examinations of the patients' stools in the hospital itself, and we were therefore compelled to do our own part of the work in London. Samples of fresh fæces from the cases to be examined were therefore collected every morning at Epsom, and sent immediately to St. Mary's Hospital and the Wellcome Research Bureau, at which places respectively we at once made the bacteriological and protozoological examinations. The organization of this daily service of specimens on a large scale, and with proper precautions to ensure the prompt delivery and authenticity of all samples examined, was again the work of Major Stephens, whose constant care and supervision in this respect have contributed materially to the success of the undertaking.

Since individual participation in the work as a whole has thus been circumscribed, we have thought it best to present our results in the form in which they now appear—each of the joint workers in the investigation assuming authorship for that part of the work only for which he or she has been responsible.

It remains only for us to add a few grateful acknowledgments, on behalf of all the authors of the present Report, for the assistance which we have received from others. To Colonel A. L. A. Webb, C.M.G., of the War Office, we are greatly indebted not only for the sympathetic interest which he has taken in our work, but also for permission to carry it out in the way which we desired, and for much assistance to that end. We are also much indebted to Capt. S. R. Douglas, I.M.S. (ret.), and to Capt. L. Colebrook, R.A.M.C., for assistance from time to time in the bacteriological work at St. Mary's Hospital. Our thanks are also due to Dr. D. G. Sutherland for much help in the routine bacteriological examinations. At Epsom Major S. Elgee, R.A.M.C., Registrar at the Manor Hospital, has given his assistance in keeping and compiling the numerous records, and Dr. C. Ormerod and Dr. T. M. O'Donnell have aided us in the wards. To all these gentlemen we offer our sincere thanks for the help which they have given us.

A word of thanks must also be said to the Wellcome Bureau of Scientific Research, which has helped us materially, in organizing and carrying out a part of our work, by affording us laboratory accommodation and assistance; and to Company Quartermaster-Sergeant E. G. Laing, Corporal H. F. Ball, and Lance-Corporal L. Burling, who have displayed both keenness and efficiency in dealing with the large amount of clerical work inseparable from an investigation of the present character.

I.

THE BACTERIOLOGICAL FINDINGS.

By

H. S. GETTINGS.

In reporting on the bacteriological examinations of the cases at the Manor War Hospital, it may at once be remarked that the result was a negative one ; for out of the 2,700 examinations on the 1,300 patients, in no case were bacilli found of the *B. dysenteriae*, *paratyphosus* or *typhosus* strains. Bacilli giving their cultural reactions were met with, but as all failed to agglutinate in the standard sera they were not accepted.

The technique adopted was based on that used by Lewis, Graham-Smith and others in their work on epidemic diarrhoea for the Local Government Board in 1910-13, (1). This method has the advantage that instead of confining the search to certain classical and well recognised strains, the whole of the lactose non-fermenting and gelatine non-liquefying aerobic intestinal bacilli met with are investigated, and by their action on certain sugars classified into groups under a rapid and easily understood system. Lewis's description (2) will best explain it. "The groups are arranged according to the action of the organisms on glucose, mannite, dulcitate, saccharose and salicin taken in succession. The scheme will be readily comprehended from the following table.*

TABLE 1.

Group.	Glucose.	Mannite.	Dulcitate.	Saccharose.	Salicin.
A	—	?	?	?	?
B	A	—	?	?	?
C	A	A	—	?	?
D	A	A	A	—	?
E	A	A	A	A	—
F	A	A	A	A	A
G	AG	—	?	?	?
H	AG	AG	—	?	?
I	AG	AG	AG	—	?
J	AG	AG	AG	AG	—
K	AG	AG	AG	AG	AG

* In this table, A and G denote respectively that acid or gas is produced by the organisms in the culture medium.

Thus Group A includes those organisms which do not ferment glucose, their action on the other four substances not being predicated.

Group B comprises those organisms which give acid with glucose but not with mannite.

The organisms of Group C give acid with glucose and mannite but not with dulcitol, and so on through Groups D and E to Group F, which contains the bacilli producing acid from each of the five substances.

The succeeding Groups G to K similarly comprise the acid and gas-forming organisms, Group G giving acid and gas with glucose but not with mannite, while Group H gives acid and gas with both of these but not with dulcitol, and so on to Group K in which all the organisms give acid and gas with all five substances."

In the original technique (3) further differentiation took place according to the possible reactions in the remaining substances in a group when such has not been predicated. Thus B. Flexner, which gives acid in glucose and mannite only, comes into Group C and is classed as Ca; while an organism which gave acid in saccharose and salicin in addition would be Cb and so on through the variations. For instance, Strong's bacillus of dysentery which differs from Flexner's in fermenting saccharose would be classed as Ce. However, this further differentiation was not used in the present work as the sub-groups met with have not been numerous. In addition to the above *primary* reactions, Lewis used eleven further sugars and got the *secondary* ones, thus obtaining the full series of reactions of the organisms tested, and allowing a very complete examination to be made. In the present investigation this also was omitted.

In the full technique all organisms had ten days in lactose peptone water at 37°, and a month on gelatine at room temperature, before the selected lactose non-fermenters and gelatine non-liquefying organisms were inoculated into the five sugars. But in the present work this had to be modified as time did not permit the above period being taken, so accordingly the gelatine test was cut out altogether and the following method adopted. An emulsion of the faeces was plated out on McConkey's bile salt lactose neutral red agar and incubated at 37° for 24 hours. One or more white colonies, if present, were picked off into lactose peptone water and incubated for 3 days. Those tubes showing no fermentation were then inoculated into the five sugars and given four days incubation, the lactose tube going back with them. At the end of that period the lactose non-fermenters which fell into Groups B (Shiga type), C (Flexner-Typhoid), or I (Paratyphoid), were then tested for agglutination against standard specific sera. The results of the total examinations may be tabulated as follows :—

TABLE 2.

Total cases examined = 1,300.

Cases showing lactose non-fermenters = 167 or 12·8 per cent.

Numbers and grouping of the lactose non-fermenters.

Group.	Type of organism.	Nos. found.	Per- centage.
A	<i>B. fecalis alk.</i> and <i>B. pyocyaneus</i> ...	23	13·7
B	<i>B. dysenteriae</i> Shiga	4	2·4
C	<i>B. dysenteriae</i> Flexner and <i>B. typhosus</i>	6	3·6
D	Unnamed	13	7·8
E	Unnamed	7	4·2
F	<i>B. tangallensis</i> (Castellani)	1	0·6
G	Morgan's Bacillus	23	13·7
H	<i>B. of epidem: jaundice</i> and <i>B. asiaticus</i>	55	32·9
I	<i>B. paratyphosus</i>	19	11·3
J	<i>B. pseudo-asiaticus</i>	12	7·1
K	Unnamed	4	2·4

Special attention was paid to Groups B, C and I, as has been previously stated. In the four instances in which Group B occurred glucose was the only sugar fermented, and all were negative to a Shiga-agglutinating serum. Further work showed that two only were non-motile and indol negative, one was non-motile and indol positive, and the fourth was motile and indol positive.

The six examples of Group C gave acid in glucose and mannite only, these being the reactions of the Flexner-Y types of *B. dysenteriae*. All, however, failed to show any agglutination in the sera. They were non-motile organisms and indol positive.

Group I gave some trouble as it appears to include a large number of "late lactosers." These on first isolating passed the seven days' test in lactose peptone water; but after keeping for a few weeks, and sub-cultivating, would then ferment the lactose in 3 to 5 days. Originally, nearly 50 organisms were classed as belonging to this group, but on being re-examined later only 19 were found to be true lactose non-fermenters. All failed to agglutinate with paratyphoid serum, and on later investigation the greater proportion were found to be motile and indol-producing. Six of the 19 fermented salicin in addition to glucose, mannite, and dulcitol, this being the reaction of Castellani's *B. columbense*, an organism which he describes as giving rise to a typhoid-like illness.

With regard to the high occurrence of Group H, it is of interest to note that Douglas and Colebrook in their recent work on dysentery patients from the Eastern Mediterranean (4) record this group as the most frequent they met with, and they bring forward evidence as to its pathogenic action on the intestine.

In the present series, out of the 55 organisms belonging to Group H, nine fermented saccharose in addition to glucose and mannite, thus corresponding—save that the gelatine reaction was not known—to Castellani's *B. asiaticus*, which he regarded as a definite diarrhoeal organism. With regard to the other groups it is to be regretted that they were not more completely investigated, but the pressure of work at the time prevented this. The work necessary for the early and punctual rendering of reports of the patients to the military authorities necessarily came first, and such research could only be attempted as would not interfere with this.

The failure to obtain any positive results from the examination of such a large number of cases would appear to indicate that, in young men under good conditions, bacillary dysentery is rapidly shaken off, and that consequently a carrier or chronic case is a rarity. This conclusion may be contrasted with that drawn from a study of bacillary dysentery in asylums, where chronic cases are far from uncommon. It is not fair, however, to compare the disease as met with among lunatics—many of them old and feeble, and all leading confined institution lives—with the disease as it affects the army. This forms a very special section of the population, consisting for the most part of young male adults, selected for their good health, kept in fit condition, and, when they acquire infection, treated under the best hygienic conditions. In such circumstances we may readily conceive that the cases of pure bacterial infection would tend to undergo rapid and complete recovery.

Such considerations naturally lead one to question the necessity of re-examining all cases which have been discharged from hospital as "negative" after careful bacteriological examination. To keep them waiting at a dépôt for further bacteriological examination is not only wasteful of the time, labour and material of the bacteriologist, but it is also a military waste in that fit men are kept out of the ranks for varying periods of time, and are not returned, as they ought to be, with the least possible delay.

SUMMARY AND CONCLUSIONS.

The stools of 1,300 patients were examined bacteriologically, and lactose non-fermenting organisms were found in 167, or 12·8 per cent.

The lactose non-fermenting bacilli met with were all classified according to Lewis's method, and their relative occurrence recorded.

No *B. dysenteriae*, *typhosus*, or *paratyphosus* were found.

II. INCIDENCE OF PROTOZOAL INFECTIONS.

By

CLIFFORD DOBELL AND MARGARET W. JEPPI.

As already noted above, every one of the 1,300 cases in the present series was examined twice bacteriologically, and only classified as "negative" when no pathogenic organisms could be found on either occasion. The same routine was adopted for the protozoological examinations. No case was regarded as "uninfected" until two negative examinations of the stools had been made. For various reasons some of the patients were examined three or more times, but such cases form only a very small proportion of the whole number; and there is but one case in the whole series who was examined once only.

As a result of the protozoological examinations of the stools of all the 1,300 cases, 156 men were found to be infected with *Entamæba histolytica*. Of these, 153 may be classified as carriers, passing cysts in their fæces; two as cases of subacute infection, with loose fæcal stools containing amœbæ only; and the remaining one, at the time when he was first examined, as an acute case passing blood, mucus, and many amœbæ containing ingested red corpuscles.

Over two-thirds of the infected cases were discovered at the first examination (108 out of 156). Of the remainder, 45 were detected at the second examination, and 3 at the third. These last were found among the patients already mentioned who were examined thrice or oftener, and of whom there were only 47.

The total incidence of infection with *E. histolytica* for the whole series of 1,300 cases is therefore 12 per cent.

Since all the cases infected with *E. histolytica* were segregated and treated, and subsequently re-examined at least six times each, they form a series of cases which must be considered as more thoroughly examined than the others. In estimating the incidence of infection with intestinal protozoa other than *E. histolytica*, we shall therefore consider these two series separately. The first series consisting of 1,144 men (1,300 less the 156 infected with *E. histolytica*), which may be considered as a series examined for the most part twice each, presented the following infections:—

381 cases infected with	<i>Entamæba coli</i>	= 33.3%.
73 " " " "	<i>Entamæba nana</i>	= 15.27% (out of 478 cases).
149 " " " "	<i>Giardia</i> (= <i>Lambli</i> a)	
	<i>intestinalis</i>	= 13.02%.
108 " " " "	<i>Chilomastix mesnili</i>	= 9.44%.
2 " " " "	<i>Trichomonas hominis</i>	—
Total number of cases examined = 1,144.		

It must be noted that the percentage of infection with *E. nana* is reckoned from only the last 478 cases examined. The presence or absence of this organism was not always recorded for the earlier members of the series, and these have therefore been omitted.

In the course of making these examinations the eggs of parasitic worms were sometimes encountered. The ova of *Trichuris trichiura* (= *Trichocephalus dispar*) were found in the faeces of 46 cases, or 4 per cent.; and those of *Ascaris lumbricoides* in 11, or 0.96 per cent. The bodies called "I cysts" by Wenyon (5) were found in 24 of the cases, or 2.1 per cent.

The second series of cases, consisting of those men who were found to be infected with *E. histolytica*, and who were all examined seven times or more each, gave the following figures:—

84 cases infected with <i>Entamoeba coli</i>	= 53.8%
52 " " " <i>E. nana</i>	= 33.3%
25 " " " <i>Giardia intestinalis</i>	= 16.0%
39 " " " <i>Chilomastix mesnili</i>	= 25.0%
6 " " " <i>Trichomonas hominis</i>	= 3.8%

Total number of cases examined = 156.

In this series *Ascaris* eggs were found in 3 patients, or 1.9 per cent.; and the eggs of *Trichocephalus* in 18, or 11.5 per cent. "I cysts" were found in 5 patients, or 3.2 per cent.

It should be pointed out that many of our positive cases were infected with strains of *E. histolytica* producing cysts of small size (Cf. 6). No less than 58 out of the total of 156 cases were passing cysts with diameters of 10 μ or less, the majority of these strains having cysts with average diameters between 7 μ and 9 μ . Twelve of the cases passing small cysts also passed cysts of the larger sizes (11 μ to 15 μ); and probably each was infected with two or more strains of the parasite forming cysts of different mean size. The rest of the cases (98) passed cysts of the larger sizes only.

At first sight the percentage of infected cases in our whole series appears remarkably high. It is not appreciably lower than the percentage (12.6 per cent.) found among the cases of dysentery and enteritis invalidated to England in 1915 and 1916 from the Eastern Mediterranean area. (Cf. 7.) Our percentage should, it would seem, be very much lower than the latter, since it refers to a series of depôt cases, discharged from hospital as negative after examination and treatment, and examined by us only twice each; whilst the cases of 1915 and 1916 were hospital cases examined on an average thrice each. Allowance must, however, be made for the carriers passing only small cysts in our present series. Such infections were not included in the earlier records, and there can be little doubt that the incidence of infection previously found was for this reason too low. The only way in which we can compare the findings in the two series,

therefore, is by eliminating the infections with small cysts from our series, and then comparing the incidence of infection calculated from the remainder with that previously found. In our whole series of 1,300 cases we found 110 passing cysts of *E. histolytica* of the larger sizes (11μ to 15μ), or 8.4 per cent. This percentage is appreciably lower than that given above for the earlier hospital cases (12.6 per cent.), but is still remarkably high. It agrees fairly closely with the incidence of infection with *E. histolytica* already recorded for depôt cases at Barton. (See 7.)

We may now consider the incidence of infection with *E. histolytica* among patients invalided to England from different localities. Our patients had suffered from dysentery in various military areas before we examined them, and we detected infections with *E. histolytica* among men from every area. But it does not, of course, follow that the frequency of carriers found among the dysenteric patients from any particular locality indicates the relative prevalence of amœbic and bacillary dysentery in that locality. We can only record the incidence of infection which we have found. We have in most cases no means of judging whether the attack of dysentery for which each patient was invalided to England was, or was not, amœbic in origin. The figures available show, however, that infection with *E. histolytica* was, as would be expected, much commoner among the cases returning from tropical and sub-tropical countries than among those from the French front.

Although we attempted to obtain particulars of every case in our series we failed, unfortunately, to ascertain the localities from which 60 of them had been returned. We tabulate below details of all the other 1,240 cases :—

TABLE 3.

Dysentery contracted in	No. of cases examined.	No. of cases infected with <i>E. histolytica</i> .	% of cases infected.
France... ..	788	66	8.37
Salonica	333	63	18.92
Egypt	58	11	18.96
Gallipoli	13	3	23.07
Mesopotamia* ...	39	8	20.51
Mediterranean† ...	5	2	40.00
India	3	2	66.66
China	1	1	100.00
	1,240	156	

* Including cases from the Persian Gulf.

† Excluding cases from Salonica, Egypt and Gallipoli. One of the two infected cases from this area came from Serbia, the other from Malta.

Although the omission of 60 negative cases must necessarily make some or all of the above percentages too high, there is no reason to suppose that their inclusion would materially alter the relative values of the different categories, since there is no reason to suppose that they all came from the same place. The high percentages found for the later categories in the table are, of course, of little significance, since they are based on a very small number of cases. The most striking feature of Table 3 is the fact that the percentage incidence of *E. histolytica* infection among men returning from France is less than half that for the men from any of the other areas. Nevertheless this percentage (8.37 per cent.) is surprisingly high, especially when it is remembered that it represents only a minimum, being based on the findings from a series of cases examined but twice each.

It might be supposed that the high incidence of infection with *E. histolytica* among the French cases is due to the inclusion among them of many men who had previously become infected in areas where amœbic dysentery is endemic, and who merely relapsed on the French front. Further analysis of the French cases, however, lends no support to this supposition. Of the 66 infected cases from France, details of previous service and medical history are lacking for 2. Of the remainder (64) we find that no less than 50 had never been out of England before they went to France, and none of them had previously suffered from dysentery. The 14 other cases had previously served in tropical or sub-tropical countries where they had all suffered from dysentery. (They were made up as follows :—Three cases from Egypt, 4 from Gallipoli ; 1 each from Salonica, S. Africa, E. Africa, India, S. America ; 1 case who had been in German S.W. Africa and Egypt, and another from S. Africa, Gallipoli and Egypt.) It is evident, therefore, that the majority (at least 50 out of 66) of our *E. histolytica* carriers from the French front must have acquired their infections in France or England. These cases constitute 6.3 per cent. of the total number (788) of convalescent dysenteric patients whom we examined from the French front.

SUMMARY AND CONCLUSIONS.

1,300 patients were examined, and 156 (12 per cent.) found infected with *Entamœba histolytica*.

The incidence of infection was lower in the cases invalided from the French front (8.37 per cent.) than among those from the East and Near East (19 per cent. and upwards).

There is evidence that the majority of carriers from the French front had acquired their infections with *E. histolytica* in France or England.

III.

TREATMENT OF CASES INFECTED WITH
E. HISTOLYTICA.

By

CLIFFORD DOBELL, MARGARET W. JEPPE, AND J. B. STEPHENS.

Of the 156 patients infected with *E. histolytica*, all but three were treated with emetine bismuth iodide at Epsom. The three who were not treated were transferred elsewhere; but in place of them we found two other *E. histolytica* carriers among the patients sent into hospital suffering from malaria, and these we added to our series. The total number of treated cases was therefore 155.

In accordance with the indications of previous experience (7), a uniform method of treatment and examination was adopted. The *dose* of the double iodide administered was always the same—3 grains in one daily dose. The *first course* of treatment for every* case extended over *twelve consecutive days*, the patient thus receiving 36 grains in all of the double iodide. When subsequent courses of treatment were necessary, the same daily dosage was adhered to, but the treatment was continued generally for more than twelve consecutive days. This procedure was adopted because previous experience had shown, first, that less than 3 grains daily is usually an inadequate dose; secondly, that treatment to be successful must be continuous; thirdly, that treatment with less than 36 grains in total amount is frequently ineffective; and fourthly, that re-treatment with larger quantities of the double iodide will sometimes cure after an initial treatment with 36 grains has failed.

In order to determine the effect of treatment upon each patient's infection, the following method was used throughout. No patient was regarded as cured of his infection until *six negative examinations* of his stools had been made *after the end of treatment*—one in the first week, one in the second, and the remaining four in the third. Negative examinations made during treatment were never included, nor was the final examination ever made before the twenty-first day after the end of treatment. All the treated cases in the present series were examined in accordance with this system; the positive (uncured) cases being subjected to further treatment as soon as they were detected. This procedure was adopted because previous experience had shown, first, that negative examinations made during treatment are valueless as an index of non-infection; secondly, that less than

* One case (No. 129), as noted below, began treatment with a course of 18 doses.

six negative examinations made during less than twenty-one days after treatment are inadequate to prove the permanent disappearance of an infection with *E. histolytica*; and thirdly, that the later the examinations are made during the three weeks following treatment, the greater is their significance as evidence of permanent cure. (Cf. 7).

Although six negative examinations made in the manner just described represent the standard invariably required to establish a "cure," it was possible in some cases to make more examinations extending over a longer period. Ninety-five of the "cured" cases received only the minimum number of six negative examinations each; but the remainder were examined as follows:—

34 had 7 negative examinations each.

3	„	8	„	„	„
5	„	9	„	„	„
2	„	10	„	„	„
1	„	12	„	„	
1	„	14	„	„	
1	„	15	„	„	

The majority of the extra examinations were made in the fourth week after the end of treatment. In no case was a relapse detected as a result of these extra examinations—a fact which encourages the hope that our criterion of cure was trustworthy.

Additional evidence of the reliability of the standard of cure adopted is furnished by a study of the dates at which relapses were detected. Altogether 59 treatments in our whole series were followed by a relapse. Of these relapses—

28 were detected at the 1st examination (1st week after treatment.)

18 were detected at the 2nd examination (2nd week after treatment.)

8 were detected at the 3rd examination (3rd week after treatment).

1 was detected at the 4th examination (3rd week after treatment).

2 were detected at the 5th examination (3rd week after treatment).

2 were detected at the 6th examination (3rd week after treatment).

These figures agree closely with the expectation from those previously obtained for treatment with emetine hydrochloride administered hypodermically (see (7), pp. 45 to 47); and they confirm the conclusions there drawn that the vast majority of relapses occur before the end of the third week after treatment, and consequently that negative examinations made at this later period possess the greatest value as an index of cure.

Although all our cases were treated with a uniform daily dosage of emetine bismuth iodide, the drug was administered in several different forms, which were found to produce widely different effects both upon the amœbic infections and upon the patients themselves. Altogether five different preparations of the double iodide were tried. These were :—

- (1) Stearin-coated pills, with resin basis.
- (2) Stearin-coated pills, with soap basis.
- (3) Salol-coated pills.*
- (4) Powdered drug in small gelatine capsules (gr. i. each).
- (5) Powdered drug in large gelatine capsules (gr. iii. each).

The routine method of administering the drug was as follows :—The patients were given a good meal at 7.30 p.m., went to bed at 8.45 p.m., and were then given their dose of emetine bismuth iodide followed by a cup of hot tea. Every precaution was taken to insure that each patient actually swallowed the whole of every dose of the drug given to him; for we were, from previous experience, fully alive to the great importance of controlling all patients most carefully in this matter.

The cases treated with the first preparation (Cases 9, 42, 105) were examined daily during treatment. It was found that the drug given in this form was without effect, either upon the amœbic infections or the patients. From these results, and others like them obtained elsewhere,† we concluded that these pills were completely insoluble, and their use was accordingly discontinued.

The clinical effects observed after administration of the other preparations of the drug were similar to those already recorded for other series (cf. (7), (8), (9), (10), &c.). The small gelatine capsules caused nausea, vomiting, and diarrhœa. The vomiting usually became less frequent as the treatment proceeded, but as a rule the diarrhœa increased. Although most patients suffered discomfort during treatment, none displayed any serious constitutional symptoms; and almost without exception the patients stated, two or three weeks after treatment, that they felt very much better. The salol-coated and stearin-coated (soap basis) pills caused comparatively little sickness, and a variable but slighter amount of diarrhœa. The large gelatine capsules produced effects unlike the small, their administration being followed by vomiting and nausea but comparatively little diarrhœa.

When vomiting occurred it was usually two or three hours after the administration of the double iodide, and it did not persist for more than a few hours. It did not interfere to any great

* The vast majority (all but three patients) were treated with salol-coated pills made with a gum basis. The three exceptions received pills made with a soap basis. As no differences of any sort were observable in the effects, all patients treated with salol-coated pills have been considered together.

† See (9), Table 4. The pills used in the treatment of all these cases were obtained from the same source.

extent with the night's rest, and the patients usually had excellent appetites throughout the day. In no case did the vomiting produce symptoms sufficiently severe even to raise the question of the advisability of discontinuing treatment, or of giving opium; and no real efforts were therefore made to discover means of preventing or alleviating the sickness. The diarrhoea usually began about the fourth day of treatment, and generally ceased about two days after its termination.

Cases suffering from chronic gastritis—of which there were several in the present series—did not appear to suffer any greater inconvenience than the others; and from our experience, therefore, it seems justifiable to conclude that the drug is not contra-indicated in the treatment of such cases.

We shall begin the account of the comparative effects of the various preparations of the double iodide upon the *E. histolytica* infections by considering what may be called the *original treatments*. By this term we mean the first course of treatment carried out by us with any form of the drug. (Some of these cases had previously been treated with emetine in other ways elsewhere). The three treatments with insoluble pills noted above have been left out of account, and the first subsequent course of treatment undergone by these three patients counted as their first. The results obtained in the original treatments of all the cases treated (155) are shown in the following table:—

TABLE 4.

Original Treatments.

(All cases treated with 3 grains emetine bismuth iodide daily for 12 consecutive days, = 36 grains in all.)

Preparation.	No. of cases			% cured.
	Treated.	Cured.	Not cured.	
Stearin-coated pills, soap basis ...	3	1	2	33.3
Salol-coated pills ...	59*	43	16	72.8
Gelatine capsules (small)...	70†	63	7	90.0
Gelatine capsules (large)...	20	11	9	55.0
Gelatine capsules (small) and salol-coated pills (mixed treatment)	3‡	3	0	100.0
	155	121	34	

* Including one case (No. 129) which received 54 grains as an original course of treatment. This was because it was found that this patient had previously been treated, without success, with a course of 36 grains elsewhere.

† Including 3 cases which each received 11 doses small gelatine capsules and 1 dose salol-coated pills.

‡ Cases 21, 35, 88. Two of these (35 and 88) received 4 doses small gelatine capsules and 8 salol-coated pills each. The other (21) had 7 doses gelatine capsules and 5 salol-coated pills. These cases were so treated merely because the supply of gelatine capsules—with which they began treatment—gave out before treatment was completed.

The number of cases treated with stearin-coated pills and by mixed treatment (3 of each) is too small to afford any certain conclusions. But whilst the results obtained with the former are distinctly unpromising, the very high percentage of cures with the latter is probably devoid of significance. We shall not discuss these further.

The results obtained with the small gelatine capsules and the salol-coated pills agreed closely with our expectation from previous experience.* They show clearly, we think, that thorough treatment with a full course of the drug (36 gr.) in a readily available form (loose powder in an easily soluble capsule) will cure, at the first trial, about 90 per cent. of the cases treated. They also show that salol-coated pills are distinctly inferior in their efficacy. A fuller discussion of these conclusions will be given below.

The large gelatine capsules, when compared both with the small and with the salol-coated pills, show a surprising inferiority to both. It is to be noted that the large capsules not only failed to rid a very high percentage of patients of their infections, but they also—as noted above—produced less diarrhoea than the small capsules. It can hardly be doubted that they were, in some way, greatly inferior in activity to the latter. For this reason we have considered the two series of treatments separately.

We had previously supposed that all treatments with the double iodide powder enclosed in gelatine capsules could be regarded as equivalent; that is to say, as treatments in which the drug was administered in exactly the same way. It seems clear, however, that we cannot without further evidence make this assumption. Several different factors may possibly have determined the difference in the results which we have noted above; and although we are unable to decide the matter definitely, we may make the following suggestions:—

(a) We think it unlikely that the administration of three grains of the powdered drug in a single large capsule, and of the same quantity of the same powder in three separate small capsules, could produce conspicuously different results. Our previous experience is wholly against this assumption.

(b) It is possible that the gelatine of which the large and small capsules were made differed in solubility, and hence that the drug was more easily available in one than in the other. In the present case we have no evidence that this is so; but we may point out that it has recently been stated (11) that certain soft gelatine capsules are much less soluble than hard capsules,

* It may be noted that our expectations in no way prejudiced our findings. All cases were examined with equal care, and in almost every instance the examiners of the stools were ignorant of the form of drug administered until after the results had been reported.

and appear to have been responsible for a similar diminution in the efficacy of certain drugs administered for ankylostomiasis.

(c) It is possible that different samples of emetine bismuth iodide contain different proportions of emetine. There is already some evidence to support this supposition, but unfortunately no analysis of the samples of the drug used in our treatments was made. If the difference in emetine-content were considerable, it would readily account for our results.

(d) It is possible that there is a qualitative difference in the emetine present in different samples of the drug. We know, however, of no evidence that different samples of pure emetine possess different efficacy in ridding a patient of an amoebic infection, though there is, we believe, some evidence that different specimens of emetine may differ in toxicity. At present it is not possible to determine which, if any, of the foregoing factors may have been responsible for the effects which we have observed.*

We have now to consider the subsequent treatments of those cases which were not cured by their original courses. It will be seen (Table 4) that altogether 34 cases were not cured originally. Of these one case (No. 157) was transferred to another hospital and not re-treated by us. Our re-treated cases number, therefore, 33 in all. After a second course of treatment some of these cases were still uncured, and were therefore given a third course, and three of them eventually a fourth. As already noted, the general principle adopted was to increase the quantity of emetine bismuth iodide at each re-treatment—the same daily dose being adhered to, but the course of treatment extended over a longer period. As re-treatments were carried out with various forms of the drug, we think it necessary to record in detail the method of treatment on each occasion for each of our 33 re-treated relapse cases. For convenience we have tabulated all the treatments undergone by each patient, together with the result of the final course of treatment, in a single table (Table 5). In this table the following abbreviations are used. The letters indicate the form in which the emetine bismuth iodide was administered, and the figures the total quantity of the drug given in consecutive daily doses of 3 gr. each.

- G.l. = Large gelatine capsules.
- G.s. = Small gelatine capsules.
- S. = Salol-coated pills.
- St. = Stearin-coated pills (soap basis).

* Another possible explanation of the apparent inferiority of the large capsules also occurred to us. It seemed possible that the patients, if they were attempting to evade treatment by not swallowing their doses, would find it easier to accomplish this with a single large capsule than with three small ones. In the later treatments with the large capsules, therefore, they were administered in a spoonful of jam, and every precaution taken to see that the dose was swallowed. The results, however, were no more satisfactory.

Thus, for example, "G.s. 72" denotes that the patient received a course of treatment consisting altogether of 72 grains of the double iodide in small gelatine capsules, given in daily doses of 3 grains for 24 consecutive days.

TABLE 5.
Treatments of 33 cases which relapsed after a first course
(gr. 36 E.B.I.).

Case No.	Courses of Treatment.				Result of final treatment.
	1st.	2nd.	3rd.	4th.	
13	St. 36	S. 36	S. 60		Cured.
18	S. 36	G.s. 45			Cured.
22	G.s. 36	S. 54			Cured.
29	G.s. 36	S. 54	G.l. 54	G.s. 72	Not cured.
39	G.l. 36	G.s. 72			Not cured.
41	S. 36	G.s. 45			Cured.
42	S. 36	G.l. 54	G.s. 72		Not cured.
45	St. 36	S. 36			Cured.
52	S. 36	S. 54	G.s. 54	G.s. 72	Not cured.
58	G.l. 36	G.s. 72			Cured.
63	G.s. 36	S. 54	G.l. 54		Not cured.
77	G.s. 36	S. 45			Cured.
78	S. 36	G.s. 45			Cured.
90	S. 36	S. 54	G.s. 54	G.l. 72	Not cured.
93	S. 36	G.l. 45			Not cured.
100	G.l. 36	G.s. 72			Not cured.
103	S. 36	G.l. 54			Cured.
108	G.l. 36	G.s. 72			Cured.
112	S. 36	G.s. 45			Cured.
118	G.l. 36	G.s. 72			Cured.
120	G.l. 36	G.s. 72			Cured.
129	S. 54	G.s. 45	G.l. 72		Not cured.
133	S. 36	S. 54			Cured.
135	G.l. 36	G.s. 96			Cured.
137	S. 36	G.s. 45	G.s. 54		Not cured.
141	S. 36	G.l. 54			Cured.
145	G.l. 36	G.s. 75			Cured.
146	S. 36	G.s. 45			Cured.
147	G.s. 36	G.l. 45			Not cured.
148	S. 36	G.s. 45			Cured.
149	G.s. 36	S. 51	G.s. 54		Not cured.
151	G.s. 36	S. 54			Cured.
152	S. 36	G.s. 45	G.l. 54		Cured.

We will now attempt to analyse the information obtainable from the results recorded in Table 5. This information is of importance from two different points of view, according as it throws light upon the problems of (A) the proportion of cases curable by a larger amount of the double iodide after a full course (36 grs.) has failed, and (B) the proportion of cases which are, for practical purposes, incurable by protracted treatment.

Although these two problems are closely correlated, it will be convenient to consider them separately.

(A) In attempting to ascertain what proportion of cases uncured by an original treatment may be cured by re-treatment with a larger quantity of the double iodide, we are confronted with the difficulty of comparing treatments in which different preparations of the drug were used. If, for example, the observed difference in curative effect between a course of treatment with small gelatine capsules and one with salol-coated pills depends upon the fact that in the former the drug is more readily available, and therefore more of it takes effect; then it is not certain whether a case such as No. 22 (Table 5), which was not cured by a full course in gelatine capsules, but was cured by a course and a half of salol-coated pills, was actually treated with a greater available quantity of the drug at the second than at the first treatment. We have, however, some definite evidence in Table 4 of the comparative efficacy of the various preparations of the double iodide employed, and by utilizing this we can arrive at fairly definite conclusions. The evidence indicates that the small gelatine capsules are most effective in treatment, the stearin-coated pills least effective, whilst the salol-coated pills are intermediate. We shall assume, therefore, that the greatest quantity of the drug is available in the small gelatine capsules, less in the salol-coated pills, and still less in the stearin-coated pills. With regard to the large gelatine capsules we can only conclude that their effects were too uncertain for any reliable inferences to be drawn from their behaviour.

One of the cases (No. 45) in Table 5, supplies us with very uncertain evidence concerning the amount of the double iodide which was necessary to effect his cure. He was treated with a full course of stearin-coated pills, and not cured, but was subsequently cured by nominally the same quantity of the drug in pills coated with salol. All that can be concluded from this is that salol-coated pills are probably more effective than those coated with stearin—in agreement with the findings in Table 4. As the evidence obtainable from this case is therefore merely qualitative, we shall not take it into account in the following quantitative analysis.

If now we analyse the results in Table 5 in the light of the foregoing considerations, we find that we have definite evidence that 23 cases actually underwent re-treatment with a larger quantity of double iodide after a smaller had proved unsuccessful. Of these, fourteen cases (Nos. 13, 18, 41, 58, 78, 108, 112, 118, 120, 133, 135, 145, 146, 148) were cured by re-treatment at the second or third attempt; and nine cases (Nos. 29, 39, 42, 52, 90, 100, 129, 137, 149) were not cured. This represents 60·9 per cent. of cases cured by more protracted treatment, and 39·1 per cent. not cured. Nine other cases may probably be included in this series, but as the different forms of the drug given to these cases

introduce an element of uncertainty—though the final results of treatment are equally definite—it seems best to consider them in the first place separately. Of these nine cases, six (Nos. 22, 77, 103, 141, 151, 152) were cured by probably a larger quantity of the drug; whereas three (Nos. 63, 93, 147) probably received a larger quantity and were not cured. The proportions cured and not cured are thus sufficiently similar to those in the first series to warrant their inclusion with them. This final series would therefore give the following figures:—

Total number of cases re-treated by larger quantities of double iodide after 36 grs.				
had failed to cure	...	...	...	32.
Number of cases cured	...	...	...	20 = 62.5%.
Number of cases not cured	...	...	...	12 = 37.5%.

It will be evident from Table 5 that the larger quantities of the drug which effected a cure were not identical in every case. Some cases were only cured after they had had a course of 72 grains of the double iodide in the form which appears, from the results of Table 4, to be the most efficient. It is possible, therefore, that those cases which remained uncured after receiving a larger quantity of the drug than was administered originally (36 grs.), but less than 72 grains in small gelatine capsules, might have been cured if treated by this latter dosage. The percentage of curable cases, therefore, may be greater than the percentage actually shown as cured by the above figures. Accordingly, it seems legitimate to conclude from our results that probably at least about two-thirds of the cases which were not cured by an initial treatment with a full course (36 grs.) of emetine bismuth iodide could have been cured by re-treatment with larger quantities.

This leads us to the consideration of the second point which we wish to elucidate.

(B) *The percentage of "incurable" cases.*—By "incurable" we mean, in the present connexion, merely that the maximum quantity of the drug usually administered (72 grs.) in its most efficient form (small gelatine capsules) failed to effect a cure. We do not imply that any of our "incurable" cases could not eventually be cured by still larger quantities of the drug. Indeed, there is perhaps some evidence that this is possible. One of our cases (No. 135, Table 5) actually received 96 grains of the double iodide during his second course of treatment. This large quantity was administered because it was found that he was still positive after taking 72 grains, and the treatment was therefore continued, without intermission, until 96 grains in all had been administered—in the hope, which was apparently fulfilled, that more protracted treatment might prove successful.

If Table 5 be consulted, it will be seen that not all of the twelve cases which remained uncured after more prolonged treatment

were shown to be "incurable" in the sense which we arbitrarily assign to this term. Actually, only five cases (Nos. 29, 39, 42, 52, 100) fall into this category, the remainder not having received a treatment of our maximum dosage and duration. Three of them (Nos. 90, 137, 149) received only 54 grains of double iodide in small gelatine capsules, though one of the three (No. 90) was subsequently given 72 grains in large gelatine capsules—a course which cannot be regarded as equivalent to 72 grains in small capsules. One other case (No. 129) had only 45 grains in small gelatine capsules followed by 72 grains in large. The remaining three cases (Nos. 63, 93, 147) are even more questionably "incurable." Two of them (Nos. 63, 147) never received more than 36 grains in small gelatine capsules. Their subsequent treatments respectively with 54 grains in salol-coated pills and large gelatine capsules (Case 63), and with 45 grains in large capsules (Cases 93, 147), cannot be regarded as demonstrating that they were "incurable." (Compare, for example, Case No. 93 with No. 41.)

To these doubtful cases we must also add, in considering our whole series, Case No. 157. This case, as already noted, was not cured by 36 grains in large gelatine capsules; but as he was not re-treated, he cannot be classified as "incurable."

Considering our 13 uncured cases in the foregoing manner, we therefore find that five (Nos. 29, 39, 42, 52, 100) were definitely "incurable"; four (Nos. 90, 129, 137, 149) were possibly "incurable"; whilst the facts about the other four (Nos. 63, 93, 147, 157) are too equivocal for definite conclusions to be drawn from them. The number of cases actually shown to be "incurable" is therefore 5, or 3.2 per cent. of our whole series of 155 cases treated for infection with *E. histolytica*. This is, of course, the minimum percentage of the "incurable" cases in our series. The maximum number of "incurable" cases is 13 out of 155, or 8.4 per cent.—the total number of cases actually left uncured at the end of this investigation. As already noted there is good reason to suppose that this percentage is too high, since there is no good evidence that at least 4 of our 13 uncured cases are incapable of being cured by adequate re-treatment.

Further information concerning the probable percentage of "incurable" cases can be obtained from a differential consideration of the results of re-treatment (Table 5) of those cases which relapsed after a first treatment (Table 4). As would be expected, there is some indication that the less efficient the original treatment is, the greater is the proportion of curable cases among those which relapse. The evidence for this is, however, by no means conclusive, since the re-treatment of the relapse cases in the several series was carried out with different quantities of the drug administered in different forms. In a previous paragraph we concluded that probably about two-thirds at least of the cases which relapsed after an original treat-

ment could be cured by more prolonged re-treatment. But since this figure was obtained by considering together all cases which relapsed after first treatments of unequal efficiency, it is clear that it cannot properly be applied to the cases which relapse after any particular and uniform method of treatment. We found (Table 4) that the most efficient original treatment was that with the double iodide powder in small gelatine capsules. Only 10 per cent. of the cases relapsed after this treatment, but for the reasons just noted we cannot conclude that two-thirds of this number could be cured by re-treatment. We can, however, obtain from Table 5 information as to the number of cases who were actually cured by treatment in various ways subsequently. Of the seven cases, three (Nos. 22, 77, 151) were cured by more prolonged treatment; one (No. 29) was "incurable" by our standard; whilst the other three (Nos. 63, 147, 149) remained uncured, but were not shown to be "incurable," none of the three having received a course of more than 54 grains of the double iodide in any form. It seems legitimate to conclude, therefore, that of the 10 per cent. of cases which were not cured originally, probably not more than one-half, or 5 per cent. of the whole series, was actually "incurable." This figure lies within the limits 3.2 per cent. and 8.4 per cent. previously given as the approximate minimum and maximum values for the number of "incurable" cases. Since there is some reason to suppose that the minimum value is too low and that the maximum may be too high, it seems justifiable to conclude that the intermediate value just ascertained (5 per cent.) represents an approximation to the truth.

From the foregoing figures we conclude, therefore, as follows. A full course of treatment (36 grs.) with emetine bismuth iodide administered in its most suitable form will free the majority (probably about 90 per cent.) of carriers of *E. histolytica* of their infections. Of those cases which remain uncured after such an original course of treatment, a further number can be cured by the subsequent administration of a larger quantity of the drug. But even a quantity of the drug (72 grs.) equal to twice that originally given will not cure every carrier of his infection. There is, however, no evidence to show that the proportion of such "incurable" cases is greater than 5 per cent. of all infected cases.

It has often been suggested (cf. 13) that cases which have previously been treated with emetine are, for that reason, more difficult to cure with the double iodide than those to whom no emetine has previously been administered. Previous experience had given no good evidence in support of this supposition (cf. 7, 12) nor of the explanation which has been advanced that the administration of emetine to a patient may render his parasites emetine-resistant. It is true that certain cases which have not been cured by treatment with emetine hydrochloride injections have subsequently also not been cured when treated with

the double iodide. But this is probably merely because these cases are difficult, if not impossible, to cure by emetine in any form. They would probably have proved just as difficult to cure with the double iodide if no other form of emetine had previously been administered. We collected particulars of previous treatment, so far as this was possible, for all our treated cases in the present series, and we will add here a few notes on certain cases in illustration of what has just been said.

Among our "incurable" patients, Case 42 had previously received 6 courses of emetine injections in India; Case 29 had had altogether 48 injections; and Case 52, 36 injections. On the other hand, we may contrast with these Cases 4, 36, and 99, who had previously received 43, 30, and 100 injections respectively, and who were all readily cured by a single course of emetine bismuth iodide; and also Case 90, who remained uncured after receiving large quantities of the double iodide (4 courses), but who had never previously been treated with emetine in any form. From facts such as the foregoing, therefore, it seems clear that no important conclusions can be drawn, though they are perfectly consistent with the view that the administration of emetine to a patient does not increase the resistance of his amoebæ to the alkaloid.

In concluding this section we may briefly refer to the effects of emetine bismuth iodide upon organisms other than *E. histolytica* with which some of the treated patients were also infected. We found no evidence that any other protozoa (*E. coli*, *E. nana*, *Lambliæ*, *Chilomastix*, *Trichomonas*) can be removed by treatment with this drug. Our experience in this respect agrees with previous observations. (Cf. 7, 12.) It is somewhat remarkable, however, and we think worthy of record, that all five cases infected with "I-bodies" lost their infections after treatment with the double iodide. Wenyon and O'Connor (14) have already recorded a similar observation made on cases treated with emetine in other forms.

What is the most effective method of treatment with emetine bismuth iodide?

Comparison of our results with those already published by some other workers supplies a partial answer to this question. There is now, we think, some fairly trustworthy evidence to show, in the first place, which form of administration of the double iodide gives the most successful results; and secondly, what method should be adopted in re-treating cases which remain uncured after a first course of treatment.

In the present paper we have given (Table 4) the comparative results obtained at Epsom by the administration of a single initial course of treatment with the double iodide in two different forms—as the powdered drug in small gelatine capsules, and as salol-coated pills. Similar results are already on record from

four other places. At Barton (8) a series of cases was treated with keratin-coated tabloids; at Bournemouth (13) another series was likewise treated with keratin-coated tabloids, and another with salol-coated pills; at Hampstead (9) and at Walton (12) two further series of cases were treated with the double iodide as a loose powder in cachets. On collecting together and analysing all the results recorded in these series we obtain the following figures :*

TABLE 6.

Form of drug employed.	No. of cases treated at					Total cases treated.	% of cases not cured.
	Barton.	Bournemouth.	Epsom.	Hampstead.	Walton.		
Keratin-coated tabloids	101	79	—	—	—	180	31·1
Salol-coated pills ..	—	25	59	—	—	84	28·6
Powder (in gelatine capsules or cachets) ..	—	—	70	11	17	98	8·2

With the exception of 24 cases in the Barton series who were cured with a smaller quantity, and two cases who were not cured by a larger, all the cases in this table were treated originally with a full course (36 grs.) of the double iodide. In this respect the three series of treatments are therefore fairly closely comparable. There is, however, another factor which must be taken into account in considering the results. The standard of non-infection for "cured" cases has not been uniform throughout, and it would therefore be expected that those series which were most thoroughly examined after treatment would show, for this reason, the highest percentages of uncured cases. The figures from Barton and Bournemouth appear to support this conclusion. At the latter place the treated cases were examined more frequently and for a longer period after treatment than at the former; and we find that, of the cases treated with keratin-coated tabloids, 82·2 per cent. were "cured" at Barton, and only 51·9 per cent. at Bournemouth. Whilst we fully appreciate the importance of such a source of error in comparing the results of different methods of treatment, we may point out that the very low percentage of cases "not cured" in the last series in Table 6 cannot be explained in this manner. For we have reason to believe that the cases included in this series were not less thoroughly examined than the others.

* In compiling this table we have excluded one case (No. 899) from the Barton series, as he relapsed after treatment with less than a full course (36 grains) of the double iodide; and for reasons given above, we have not considered the Epsom cases treated with powder in *large* gelatine capsules.

It seems to us legitimate to conclude, therefore, both from our own results and from those of others, that the most effective of the methods here considered of treating amoebic dysentery carriers with the double iodide of emetine and bismuth, is to administer the drug in the form of a loose powder in a gelatine capsule or cachet, and not as a compressed pill or tablet coated with salol or keratin.* This conclusion is in complete agreement with our own previous experience, and with that already recorded by Low (15).

With regard to the best method of re-treating cases which remain uncured after an original full course of treatment with the double iodide, we would note the following points. From earlier experience (7) it appeared probable that the most successful results could be obtained by increasing the amount of the drug administered for the second course of treatment. All the treatments in the present series were carried out in accordance with these indications, and it will be remembered that we cured, by this procedure, about one-half to two-thirds of the cases remaining uncured after a first course. At Bournemouth, however, the system was adopted (13) of re-treating the uncured cases with a second course of the double iodide of the same quantity as was used originally (36 grs.). By this method 8 cases out of 38, or 21 per cent., were ultimately cured—a result which appears less successful than our own. It seems to us probable, therefore, that the method which we adopted gives promise of the better results.

We have still to consider what quantity of the double iodide should be administered at the second course. After considering the results recorded in Table 5 we have come to the conclusion that the second course of treatment should be carried out with twice the quantity of the drug (72 grs. in 24 days), that was administered in the first course (36 grs. in 12 days). Re-treatment with courses extending over 15 days (45 grs.) or 18 days (54 grs.) cured comparatively few additional cases, and consequently necessitated the retention in hospital of many patients, and their further re-treatment with longer courses at a later date. It seems probable, therefore, that the administration of a full double course of emetine bismuth iodide (3 grains daily for 24 consecutive days = 72 grains in all) will cure, in the minimum length of time, the maximum number of those cases which, after a single first course of treatment (36 grains in 12 days), remain still uncured.

SUMMARY AND CONCLUSIONS.

One hundred and fifty-five amoebic dysentery carriers were treated with emetine bismuth iodide, administered in various forms, and in doses of 3 grains daily for 12 or more days consecutively.

* Or, we may add, with stearin. Cf. the results recorded earlier in the present Report, and those recorded at Hampstead (9).

One hundred and forty-two cases (91.6 per cent.) were finally discharged as cured. Analysis of our findings indicates that the most successful results were obtained by administration of the drug as an uncompressed powder in gelatine capsules. A single first course of treatment (3 grains daily for 12 consecutive days = 36 grains) cured 90 per cent. of the cases so treated.

When cases remain uncured after such treatment the best method of re-treating them is to give them a double course of the drug (3 grains daily for 24 consecutive days = 72 grains).

Such treatment has not cured every case; but there is no evidence that those which are not curable by this means constitute more than 5 per cent. of all carriers of *E. histolytica*.

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